THESIS

ELECTRODIFFUSION ON THE SURFACE OF BILAYER MEMBRANES

Submitted by

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ABSTRACT

ELECTRODIFFUSION ON THE SURFACE OF BILAYER MEMBRANES

The cell memebrane is of utmost importance in the transportation of nutrients to the cell which are needed for survival. The magnitude of this is the inspiration for our study of the lipid bilayer which forms the cell membrane. In this paper we present a continuum model of electrodiffusion of lipids on the surface of bilayer membranes. Offering three derivations of the surface electrodiffusion equation, and proofs for the existence and uniqueness of the solution. A method for calculating integration constants using slotboom variables is emloyed. The development of a linear surface finite element method to solve the surface electrodiffusion equation is presented. Numerical simulations implementing the model are also given. The stability of the model is analyzed and a stability scheme using Streamline Upwind Petrov-Galerkin equations is applied. We test our code for robustness using other examples and a complex mesh. The implementation is validated by comparing with the known solution for the equations.

TABLE OF CONTENTS

Chapter 1

INTRODUCTION

Although cell membranes have been studied since 1855, introduced by C.Naegeli and C.Cramer, the present membrane model was not developed until 117 years later. The first fluid mosaic model (Figure 1.1) of a biological membrane was developed by Singer and Nicolson. The general model only differs for individual cell membranes by lipid types or lipid to protein ratios. Since 1972 there have been some changes to the fluid mosaic model. Such as

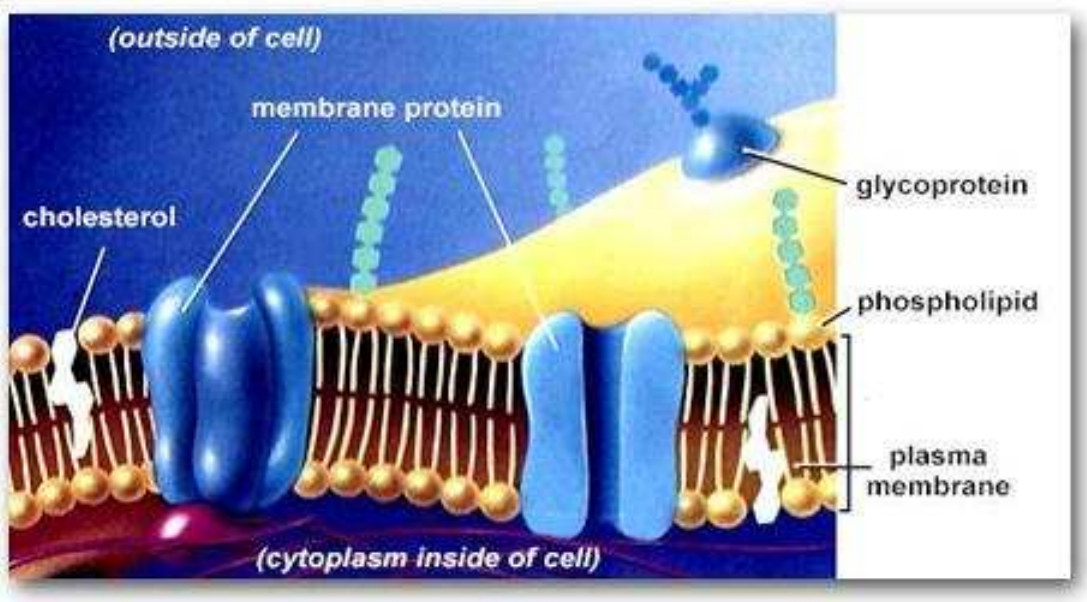

Figure 1.1: Fluid Mosaic Model

the memebrane having a patchwork mesh such that inside the patches lipid movement occurs [11], instead of lipids moving freely across the entire cell surface [11]. The cell membrane is differentially permeable and regulates what enters and exits the cell. To understand the form and stability of a cell membrane the knowledge of lipid behavior is essential, since the cell membrane is made of a lipid bilayer with embedded proteins. The lipid bilayer is formed by the spontaneous self arrangement of phosopholipids, so that their tails are isolated from

the surrounding aqueous solution. This arrangement leaves their heads free to associate with other surfaces. In aqueous solutions lipids are able to laterally exchange locations with their neighbors (Figure 1.2). This movement happens often, in fact millions of times a second [1]. Another type of movement, that happens much more slowly and not as often, is a lipid flip-flop (Figure 1.2). This occurs when a lipid crosses the hydrophobic membrane core. This rare event has many degrees of freedom and multiple time scales which make it very difficult to understand and model. Despite being the least understood dynamical process in the membrane, there are currently some simple models using transition path sampling (TPS) of this biological phenomena [9].

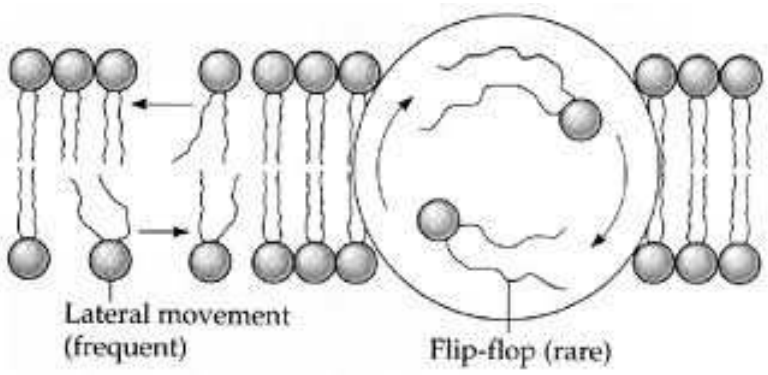

Figure 1.2: Lipid Movements

The lateral exchange resembles a random walk on the membrane surface which is mathematically equivalent to lateral diffusion on the membrane surface. Van der Waals, electrostatic, hyrdogen bonds, and noncovalent interactions are some of the forces associated with lateral diffusion and the formation of the lipid bilayer. These forces motivate the study of surface diffusion of lipids on membrane surfaces. The first mathematical paper written on this subject was in 1988 by Gerhard Dziuk [3]. It introduced the use of the Laplace-Beltrami operator, Δ_s, to model diffusion on surfaces.

$$D\Delta_s u = f \quad on\ \Omega \tag{1.1}$$

Where u is the concentration of lipids on an arbitrary surface, Ω. D is the diffusion coefficient. f is the production/destruction of lipids, and $\Delta_s = \nabla_s \cdot \nabla_s$ where ∇_s is the tangential gradient on Ω which represents the net rate at which a lipid moves on the surface. The diffusion coefficient, D, is the measure of the lipid movment around neighboring lipids and proteins [6]. Logically then, the bigger the lipid the smaller the difusion coefficient. For diffusion on spheres, one way to calculate the diffusion coefficient is using the Stokes-Einstein equation [6]

$$D\gamma = k_B T \tag{1.2}$$

Where T is the temperature in Kelvin and k_B is the Boltzmann constant. It is important to note that the diffusion coefficient relies on the size of the lipid we are studying. For non-spherical domains there have been many studies on how to calculate this coefficient using many different techniques including TPS as observed in [9] and through Resonance Energy Transfer as in [12]. Dziuk's surface model [3] has been widely accepted and used in various applications such as hydrogen diffusion on clean metal surfaces, cesium transport, and stressed epitaxial films [10]. But, is this model accurate enough to model lipids on the membrane surface? Lipid movement is not only a result of diffusion but also from the electrostatic force given off by other lipids, protiens, and molecules. This type of movement inside a domain has been modeled using the drift-diffusion or FokkerPlanck equation (1.4) which were introduced by Adriaan Fokker and Max Planck in 1931.

$$\nabla \cdot D\left(\nabla u + qu\nabla\phi\right) - \frac{\partial u}{\partial t} = f \tag{1.3}$$

Where u is the concentrati on of lipids in a domain, D is the diffusion coefficient, q is the charge on the lipid, ϕ is the electrostatic potential, and f is the production/destruction of lipids. This equation also has many other applications, such as modeling of nano-structural defects in fusion materials, chemotaxis of biological populations, stellar dynamics, and two-dimensional turbulence [10]. But how to model this on a surface? This question is the

motivation behind the surface electrodiffusion equations.

$$\nabla_s \cdot D\left(\nabla_s u + qu\nabla_s \phi\right) - \frac{\partial u}{\partial t} = f \quad on\ \Omega \tag{1.4}$$

Where u is the concentration of lipids on the surface Ω, D is the diffusion coefficient, q is the charge on the lipid, ϕ is the electrostatic potential, and f is the production/destruction of lipids on Ω. Although lipid movement is our motivation for this model, it is useful to note that this equation can be used to model other physical phenomena. To name a few would include the modeling of surfactants which act as detergents, wetting agents, and emulsifiers,and the modeling of nano-particles which may be applied in corrosion protection, crack-resistant electrodes, and antireflective films [13]. This model and variations of this model have been investigated by scientist using different numerical methods.

The numerical techniques for solving this are generally particle-based and continuum methods. The most common particle-based methods include Monte Carlo, Brownian dynamics, and Langevin dynamics [8]. These methods follow each individual particle's trajectories, which may cause these methods to diverge when applied to large amounts of particles [8]. Continuum methods instead consider the average density distribution of charged particles using partial differential equations. These methods are also easily modified to better model physical interactions. Although, both types of methods agree qualitatively well, due to the possible divergence and computational cost of the particle-based methods it is more efficient to apply continuum methods [7]. This leads to a hightened interest in the surface finite element method. The finite element method (FEM) is a numerical technique for approximating partial differential equaions (PDE). The idea behind the method is to appoximate the PDE using ordinary differential equations (ODE) and then numerically integrating them over a polyhedral mesh. The development of FEM is credited to Alexander Hrennikoff and Richard Courant in 1941. However, the first surface FEM did not come about until 1988 when Dziuk introduced the method for solving the surface diffusion problem (1.1) [3]. He concluded that

since we can paramaterize the triangular elements of the mesh to the reference triangle in $\mathbb{R}^2$, this method is the same as in a 2D plane problem except for the storage of 3D coordinates.

Although the surface electrodiffusion equation is being used to model physical phenomena the model lacks a supportive theoretical background. This paper provides the theoretical proofs, derivations, and numerical methods needed to make the surface electrodiffusion equations a strong model for lipid diffusion on membrane surfaces. We offer three derivations of the surface electrodiffusion equation, and proofs for the existence and uniqueness of the solution. We introduce a linear surface finite element method to solve the surface electrodiffusion equation, and provide results for numerical simulations.

Chapter 2

SURFACE ELECTRODIFFUSION

2.1 Derivation of Surface Electrodiffusion

Here we present three derivations of the surface electrodiffusion equation. For all derivations let Ω be a compact two dimensional, C^3-hypersurface imbedded in $\mathbb{R}^3$. Where u is the concentration of lipids on the surface Ω, D is the diffusion coefficient, q is the charge on the lipid, ϕ is the electrostatic potential, and f is the production/destruction of lipids.

2.1.1 Derivation by Energy Minimization

The membrane free energy functional is given by

$$F = \int_\Omega (U - TS)\, ds \tag{2.1}$$

Where U is the internal energy, T is the temperature in Kelvin, and S is the entropy. This can be defined for the membrane-lipid system following the derivation given by Zhou in [15] as

$$F = k_B T \int_\Omega [u \ln(\frac{u}{\xi})]\, ds + \int_\Omega -\frac{1}{2}\epsilon|\nabla\phi|^2 + zeu\delta(x - X_\Omega)\phi\, dx \tag{2.2}$$

Where k_B, T, ϕ are the Boltzmann constant, temperature, and electrostatic potential respectively. The valences of the corresponding lipids is z and e is the elementary charge.

$$\xi = \frac{1}{a^2}$$

is the effective gas pressure of lipids approximated as hard disks with the effective size a.

$$\mu = \frac{\delta F}{\delta u} = ze\phi + k_B T[\ln(u(a^2)) - \ln(1 - u(a)^2)] \tag{2.3}$$

is the electrochemical potentials, μ , given by the variations of F with respect to u. The electrochemical potentials correspond to the flux of lipids by

$$J = -mu\nabla_s \mu \tag{2.4}$$

Where m is the mobility of the lipid. We can then use the mass conservation laws on the membrane surface to derive the electrodiffusion equations on the surface Ω.

2.1.2 Derivation by Conservation of Mass

By Fick's Law of Diffusion we know the flux, J, is the net difference over the time interval, given by

$$J = D\frac{\partial u}{\partial t}$$

where D is the diffusion coefficient. To obtain the flux for the electrodiffusion equations we add a term to account for the movement due to the external force (electrostatic potential) which would result in the lipid having a velocity, u_s [6]. With this and the flux, J, given in (2.4) we have the corresponding surface electrodiffusion equations obtained from the mass conservation on the membrane surface given by

$$\frac{\partial u}{\partial t} + \nabla_s \cdot (uu_s) + u(\nabla_s \cdot \vec{n})(u_s \cdot \vec{n}) = -\nabla_s \cdot J = \nabla_s \cdot (mu\nabla_s \mu) \tag{2.5}$$

Where $\vec{n}$ are the normal vectors to the surface Ω. Since the mobility, m, is related to the diffusion coefficient, D, referred to in (1.3), we get

$$\nabla_s \cdot (mu\nabla_s \mu) = \nabla_s \cdot D\left(\nabla_s u + \frac{kua^2\nabla_s u}{1 - a^2 u} + \frac{1}{k_B T}uze\nabla_s \phi\right) \tag{2.6}$$

where $k = \frac{a}{a_0}$ and a_0 is the effective size of the polar lipids [15]. If we consider the steady-state problem, $\frac{\partial u}{\partial t} = 0$, and we obtain

$$\nabla_s \cdot D\left(\nabla_s u + \frac{kua^2\nabla_s u}{1-a^2u} + \frac{1}{k_BT}uze\nabla_s\phi\right) = 0 \tag{2.7}$$

The second term, $\frac{kua^2\nabla_s u}{1-a^2u}$, accounts for the size of the lipid and does not allow for infinite clustering of lipids on the membrane. In this paper this term is omitted for simplicity, but is discussed further in the future works section and in [15]. Now we obtain the simple drift-diffusion equation

$$\nabla_s \cdot D\left(\nabla_s u + \frac{1}{k_BT}uze\nabla_s\phi\right) = 0 \tag{2.8}$$

Letting $q = \frac{1}{k_BT}ze$ we arrive at the desired form of the surface drift-diffusion equation

$$\nabla_s \cdot D\left(\nabla_s u + qu\nabla_s\phi\right) = 0 \tag{2.9}$$

2.1.3 Derivation by Differential Geometry

The derivation of the electrodiffusion equation using differential geometry was given by H.A. Stone in [14]. We first consider the concentration of lipids in the absence of diffusion, reaction, or any flux to the surface on a deforming surface Ω. A concentration balance is given by

$$\frac{d}{dt}\int_\Omega u\, d\Omega = 0 \quad on\ \Omega \tag{2.10}$$

where $\frac{d}{dt}$ is a material derivative. If we bring $\frac{d}{dt}$ through the integral we obtain

$$\int_\Omega \frac{du}{dt}d\Omega + u\frac{d\Omega}{dt} = 0 \quad on\ \Omega \tag{2.11}$$

The second term , $u\frac{d\Omega}{dt}$, is the deformation of the surface. Since we aren't considering a deforming surface, $u\frac{d\Omega}{dt} = 0$. However, if a deforming surface is considered, the term may

be left in and the calculations carried out as in [14]. Since u is defined only on the surface, Ω,

$$\frac{du}{dt} = \frac{\partial u}{\partial t} + v \cdot \nabla_s u$$

where

$$\nabla_s = \nabla - (\nabla \cdot \vec{n})\vec{n}$$

is the surface gradient, $\vec{n}$ is the normal vector to Ω and v is the velocity of lipids. Making these substitutions into equation (2.11) we obtain

$$\frac{\partial u}{\partial t} + \nabla_s \cdot (vu) = 0 \tag{2.12}$$

Decomposing v into components along the surface, v_s, and normal to the surface, $(v \cdot \vec{n})\vec{n}$

$$\frac{\partial u}{\partial t} + \nabla_s (u v_s) + u(\nabla_s \cdot \vec{n})(v \cdot \vec{n}) = 0 \tag{2.13}$$

Where the third term , $u(\nabla_s \cdot \vec{n})(v \cdot \vec{n})$, is a sourcelike contribution accounting for variation in surfactant concentration resulting from local changes in interfacial area [14]. Since we are working on a static membrane, $u(\nabla_s \cdot \vec{n})(v \cdot \vec{n}) = 0$, and $v_s = 0$. Now with the addition of drift-diffusion on the right hand side we obtain the desired equation.

$$\frac{\partial u}{\partial t} = \nabla_s \cdot (D \nabla_s u + Dqu \nabla_s \phi) + f \tag{2.14}$$

2.1.4 Biological Definition

We have derived the follwing drift-diffusion equation

$$\nabla_s \cdot D\left(\nabla_s u + qu \nabla_s \phi\right) - \frac{\partial u}{\partial t} = f \quad on\ \Omega \tag{2.15}$$

Now breaking down each component:

1. $\frac{\partial u}{\partial t}$ is the change in the lipid concentration over time.
2. $D\nabla_s u$ term accounts for the diffusion flux of lipids on the surface as discussed in the introduction
3. $Dqu\nabla_s \phi$ is the drift flux that accounts for the movement of the lipid due to the charge given off by the electrostatic potential, ϕ
4. f is the source term or the production/destruction of lipids. This could be caused by the "flip-flop" movement discussed in the introduction or by endo/exocytosis

Combining each term gives us the movement of lipids on the surface of the cell membrane in an aqueous solution.

2.1.5 Surface Gradient

If we are able to extend the surface Ω then let d be some oriented distance function defined on some open set $U \subseteq \mathbb{R}^3$, then Ω may be written as

$$\Omega = \{x \in U | d(x) = 0\} \tag{2.16}$$

where $\nabla d \neq 0$ and $\partial\Omega = \emptyset$ [3]. Then the tangential gradient on Ω can be written as

$$\nabla_s u = \nabla u - (\nabla u \cdot \vec{n})\vec{n} \quad \in \mathbb{R}^3 \tag{2.17}$$

For $u \in C^1(\Omega)$, where ∇ is the three-dimensional gradient and $\vec{n}$ is the normal vector to Ω. For smooth Ω we may assume that there is a strip

$$U = \{x \in \mathbb{R}^3 | \, dist(x, \Omega) < \delta\}$$

about Ω where

$$x = a(x) + d(x)\vec{n} \tag{2.18}$$

is unique [3]. Where $a(x) \in \Omega$ and $|d(x)| = dist(x, \Omega)$. So we may uniquely extend a function u defined on Ω to U by

$$\hat{u} = u(x - d(x)\vec{n}) \ , \ x \in U \tag{2.19}$$

If we are unable to extend the surface, Ω to U then let $c(t)$ be a curve defined on the same Riemannian manifold as that defined by Ω. Then $c(t) = \Omega(u(t), v(t))$ where $u(t), v(t)$ are tangent vectors to the surface Ω then by taking the derivative of $c(t)$ we obtain

$$c'(t) = \frac{\partial \Omega}{\partial u}\frac{du}{dt} + \frac{\partial \Omega}{\partial v}\frac{dv}{dt} \tag{2.20}$$

If $s(t)$ represents the arc length of the curve then

$$s(t) = \int_a^b |c'(t)|\, dt \tag{2.21}$$

and

$$\frac{ds}{dt} = |c'(t)| \tag{2.22}$$

Which means

$$\begin{aligned}
\frac{ds}{dt}^2 &= |c'(t)|^2 \\
&= \left(\frac{\partial \Omega}{\partial u}\frac{du}{dt} + \frac{\partial \Omega}{\partial v}\frac{dv}{dt}\right)^2 \\
&= \left(\frac{\partial \Omega}{\partial u}\frac{du}{dt}\right)^2 + 2\left(\frac{\partial \Omega}{\partial u}\frac{du}{dt} \cdot \frac{\partial \Omega}{\partial v}\frac{dv}{dt}\right) + \left(\frac{\partial \Omega}{\partial v}\frac{dv}{dt}\right)^2
\end{aligned}$$

If we let

$$g_{1,1} = \left(\frac{\partial \Omega}{\partial u}\right)^2$$
$$g_{2,2} = \left(\frac{\partial \Omega}{\partial v}\right)^2$$
$$g_{1,2} = \left(\frac{\partial \Omega}{\partial u} \cdot \frac{\partial \Omega}{\partial v}\right)$$
$$g_{2,1} = \left(\frac{\partial \Omega}{\partial v} \cdot \frac{\partial \Omega}{\partial u}\right)$$

Then the metric tensor g is given by

$$g = \begin{bmatrix} g_{1,1} & g_{1,2} \\ g_{2,1} & g_{2,2} \end{bmatrix} \tag{2.23}$$

Note that this matrix is symmetric, since $g_{2,1} = g_{1,2}$. Using this we can compute g for any paramaterized surface [15]. Then we have the following definitions

$$\nabla_s u = \frac{1}{\sqrt{g}} \frac{\partial}{\partial x^i} u^i \sqrt{g}$$
$$\Delta_s u = \nabla_s \cdot \nabla_s u = \frac{1}{\sqrt{|g|}} \frac{\partial}{\partial x^i} (\sqrt{|g|} g^{ij} u)$$

2.2 Uniqueness Constraints

For enclosed membrane surfaces the electrodiffusion equation does not have boundary conditions, but is subject to the constraint of mass conservation

$$\int_\Omega u \, ds = T \tag{2.24}$$

Where T is the given total quantity of charged lipids on the surface Ω. In this paper we study the steady-state electrodiffusion equation which implies $\dfrac{\partial u}{\partial t} = 0$ and we assume there

is no source term, $f = 0$, so the equation becomes

$$\nabla_s \cdot D(\nabla_s u + qu\nabla_s \phi) = 0 \tag{2.25}$$

Note that if the mass conservation constraint is neglected the result is the trivial solution $u = 0$. To avoid this we introduce a decomposistion (2.26) that will result in a physical solution.

$$u = \tilde{u} + \bar{u} \tag{2.26}$$

where

$$\bar{u} = \frac{T}{\int_\Omega ds} \tag{2.27}$$

is the average concentraion of u on the surface Ω and $\tilde{u}$ is the nontrivial variation of u to be solved. Implementing this decomposition gives us

$$\nabla_s \cdot D(\nabla_s(\tilde{u} + \bar{u}) + q(\tilde{u} + \bar{u})\nabla_s \phi) = 0 \tag{2.28}$$

Reducing the equation to the simplest form gives us the following

$$\nabla_s \cdot D(\nabla_s \tilde{u} + q\tilde{u}\nabla_s \phi) = -Dq\bar{u}\nabla_s^2 \phi \tag{2.29}$$

Since $u = \tilde{u} + \bar{u} \Rightarrow \int_\Omega u\, ds = \int_\Omega \tilde{u}\, ds + \int_\Omega \bar{u}\, ds$ and by letting $\int_\Omega ds = A$, where A is some constant, then by definition of $\bar{u} \Rightarrow \int_\Omega u\, ds = \int_\Omega \bar{u}\, ds$ and we also have the constraint

$$\int_\Omega \tilde{u}\, ds = 0 \tag{2.30}$$

Now the problem we have to solve is

$$\nabla_s \cdot D(\nabla_s \tilde{u} + q\tilde{u}\nabla_s \phi) = -Dq\bar{u}\nabla_s^2 \phi \tag{2.31}$$
$$\int_\Omega \tilde{u}\, ds = 0$$

Theorem 2.2.1. (Continuous Problem) *There exists a unique solution in* $H^1(\Omega)$ *to*

$$\nabla_s \cdot D(\nabla_s \tilde{u} + q\tilde{u}\nabla_s \phi) = -Dq\bar{u}\nabla_s^2 \phi \tag{2.32}$$
$$\int_\Omega \tilde{u}\, ds = 0$$

for any smooth ϕ *such that* $\int_\Omega \nabla_s^2 \phi = 0$

Proof. If we introduce the slotboom variables $\hat{D} = De^{-q\phi}$, $\hat{u} = \tilde{u}e^{q\phi}$ we can write (2.32) as

$$\nabla_s \cdot \hat{D}(\nabla_s \hat{u}) = -Dq\bar{u}\nabla_s^2 \phi \tag{2.33}$$
$$\int_\Omega \hat{u}e^{-q\phi}\, ds = 0$$

Since $\hat{D} > 0$ this problem is elliptic, and we can write it in a bilinear form,

$$a(\hat{u}, v) = \int_\Omega \hat{D}\nabla_s \hat{u} \cdot \nabla_s v\, ds.$$

Consider the space

$$V := \{v \in H^1(\Omega) | \int_\Omega v e^{-q\phi}\, ds = 0\}$$

Then V is closed under addition in H^1 since for $v_1 \in V$ and $v_2 \in V \Rightarrow \int_\Omega v_1 e^{-q\phi}\, ds = 0$ and $\int_\Omega v_2 e^{-q\phi}\, ds = 0$ and $v_1 + v_2 \in H^1$ since H^1 is closed and

$$\int_\Omega (v_1 + v_2)e^{-q\phi}\, ds = \int_\Omega v_1 e^{-q\phi}\, ds + \int_\Omega v_2 e^{-q\phi}\, ds = 0 + 0 = 0 \tag{2.34}$$

So, V is a Hilbert space with respect to the inner product of H^1, and if we let

$$f = \nabla_s^2 \phi$$

then the weak form of the right hand side can be written as

$$-\bar{u}Dq \int_\Omega \nabla_s^2 \phi v \, ds = -\bar{u}Dq \int_\Omega f v \, ds \tag{2.35}$$

where $v \in V$. Let $v = 1$ then

$$-\bar{u}Dq \int_\Omega f \, ds = 0$$

since

$$\int_\Omega \nabla_s^2 \phi \, ds = 0$$

Thus, by the Lax - Milgram Theorem we know there exists a unique weak solution $u \in V$ to (2.32). □

To numerically compute the solution to (2.32) we implement a linear surface finite element scheme.

Chapter 3

LINEAR SURFACE FINITE ELEMENT METHOD

To implement the surface finite element method we put equation (2.32) in its weak form by applying the surface divergence theorem.

Theorem 3.0.2. (Surface Divergence Theorem) *Let $f : S \to \mathbb{R}^3$ be a vector field defined on the smooth surface, $S \subset \mathbb{R}^3$. Then,*

$$\int_S (\nabla_s \cdot f) v \, ds = \int_{\partial S} (f \cdot \vec{m}) v \, da - \int_S f \cdot \nabla_s v \, ds \tag{3.1}$$

Where $\vec{m}$ is the normal to the boundary, ∂S, and $v \in H_0^1(\Omega)$.

We define the soblev space $H_0^1(\Omega)$ and the norm on this space that will be used through out the paper.

Definition 3.0.1. *$H_0^1(\Omega)$ is the Sobolev space defined as*

$$H_0^1(\Omega) = \{v \in H^1(\Omega) : v = 0 \text{ on } \partial\Omega, v = 0 \text{ on } \Gamma_D\} \tag{3.2}$$

where Γ_D is the Dirichlet boundary condition.[5]

Note that the norm on this space is as follows

Definition 3.0.2. *$H_0^1(\Omega)$ is the completion of $C_0^1(\Omega)$ with respect to the norm*

$$\| u \|_{H_0^1} = \int_\Omega | u | \, ds \tag{3.3}$$

for $u \in C^1(\Omega)$ [5]

3.1 Weak Form

Now letting $f = D(\nabla_s \tilde{u} + q\tilde{u}\nabla_s \phi)$ and applying Theorem 3.0.2 the electrodiffusion equation can be written in the weak form as

$$\int_\Omega \nabla_s \cdot (D\nabla_s \tilde{u} + Dq\tilde{u}\nabla_s \phi) v \, ds = \int_{\partial\Omega} ((D\nabla_s \tilde{u} + Dq\tilde{u}\nabla_s \phi) \cdot \vec{m}) v \, da - \int_\Omega (D\nabla_s \tilde{u} + Dq\tilde{u}\nabla_s \phi) \cdot \nabla_s v \, ds$$

Since we know

$$\int_\Omega \nabla_s \cdot (D\nabla_s \tilde{u} + Dq\tilde{u}\nabla_s \phi) v \, ds = \int_\Omega -Dq\bar{u}\nabla_s^2 \phi v \, ds$$

we can make this substitution to get

$$\int_{\partial\Omega} ((D\nabla_s \tilde{u} + Dq\tilde{u}\nabla_s \phi) \cdot \vec{m}) v \, da - \int_\Omega (D\nabla_s \tilde{u} + Dq\tilde{u}\nabla_s \phi) \cdot \nabla_s v \, ds = \int_\Omega -Dq\bar{u}\nabla_s^2 \phi v \, ds$$

In this paper we will consider the surface, Ω, with $\partial\Omega = \emptyset$ thus,

$$\int_{\partial\Omega} ((D\nabla_s \tilde{u} + Dq\tilde{u}\nabla_s \phi) \cdot \vec{m}) v \, da = 0$$

So we have the weak form as

$$\int_\Omega (D\nabla_s \tilde{u} + Dq\tilde{u}\nabla_s \phi) \cdot \nabla_s v \, ds = \int_\Omega -Dq\bar{u}\nabla_s^2 \phi v \, ds \tag{3.4}$$

If we apply Theorem 3.0.2 to the right hand side of this equation we obtain

$$\int_\Omega (D\nabla_s \tilde{u} + Dq\tilde{u}\nabla_s \phi) \cdot \nabla_s v \, ds = -Dq\bar{u} \int_\Omega \nabla_s \phi \cdot \nabla_s v \, ds$$

Now the complete weak form is

$$\int_\Omega (D\nabla_s \tilde{u} \cdot \nabla_s v + Dq\tilde{u}\nabla_s \phi \cdot \nabla_s v)\, ds = -Dq\bar{u} \int_\Omega \nabla_s \phi \cdot \nabla_s v\, ds \tag{3.5}$$

$$\int_\Omega \tilde{u}\, ds = 0$$

where all $v \in H_0^1(\Omega)$.

3.2 Linear Surface Finite Element Method

First we approximate Ω by a polyhedral surface Ω_h which is the union of triangular faces. Let $T_j = \{P_j\}$ be the set of triangular faces as in Figure 3.1, and $P_j = \{p_k(x, y, z)\}$ be the corresponding set of vertices.

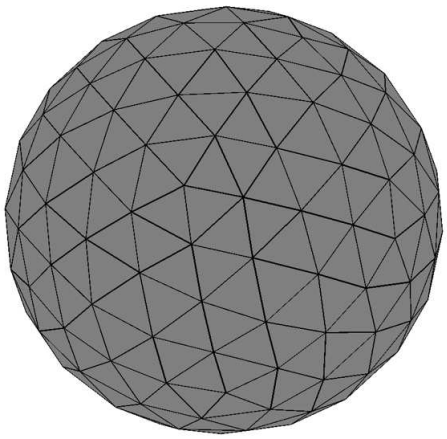

Figure 3.1: Sphere with Triangle Mesh

Thus,

$$\Omega \approx \Omega_h = \sum_j^N T_j \tag{3.6}$$

The same conclusions as in Theorem 2.2.1 hold and will proved

Theorem 3.2.1. (Discrete Problem) *For every $f_h \in L^2(\Omega_h)$ with $\int_{\Omega_h} f_h \, ds_h = 0$ there exists a unique weak solution $u_h \in H^1(\Omega_h)$ of*

$$\begin{gathered} \nabla_{s_h} \cdot D \left(\nabla_{s_h} \tilde{u} + q\tilde{u} \nabla_{s_h} \phi \right) = -Dq\bar{u} \nabla_{s_h}^2 \phi \\ \int_{\Omega_h} \tilde{u} \, ds = 0 \end{gathered} \tag{3.7}$$

on Ω_h.

Proof. If we introduce the slotboom variables $\hat{D} = De^{-q\phi}$, $\hat{u} = \tilde{u}e^{q\phi}$ we can write (3.12) as

$$\begin{aligned} \nabla_{s_h} \cdot \hat{D}(\nabla_{s_h} \hat{u}) &= -Dq\bar{u}\nabla^2_{s_h}\phi \\ \int_{\Omega_h} \hat{u}e^{-q\phi}\, ds &= 0 \end{aligned} \tag{3.8}$$

Since $\hat{D} > 0$ this problem is elliptic, and we can write it in a bilinear form,

$$a(\hat{u}, v) = \int_{\Omega_h} \hat{D}\nabla_{s_h}\hat{u} \cdot \nabla_{s_h} v\, ds.$$

Consider the space

$$V := \{v \in H^1(\Omega_h) | \int_{\Omega_h} ve^{-q\phi}\, ds = 0\}$$

Then V is closed under addition in H^1 since for $v_1 \in V$ and $v_2 \in V \longrightarrow \int_{\Omega_h} v_1 e^{-q\phi}\, ds = 0$ and $\int_{\Omega_h} v_2 e^{-q\phi}\, ds = 0$ and $v_1 + v_2 \in H^1$ since H^1 is closed and

$$\int_{\Omega_h} (v_1 + v_2)e^{-q\phi}\, ds = \int_{\Omega_h} v_1 e^{-q\phi}\, ds + \int_{\Omega_h} v_2 e^{-q\phi}\, ds = 0 + 0 = 0 \tag{3.9}$$

So, V is a Hilbert space with respect to the inner product of H^1, and if we let

$$f = \nabla^2_{s_h}\phi$$

then the weak form of the right hand side can be written as

$$-\bar{u}Dq \int_{\Omega_h} \nabla^2_{s_h}\phi v\, ds = -\bar{u}Dq \int_{\Omega_h} fv\, ds \tag{3.10}$$

where $v \in V$. Let $v = 1$ then

$$-\bar{u}Dq \int_{\Omega_h} f\, ds = 0$$

since

$$\int_{\Omega_h} \nabla^2_{s_h}\phi\, ds = 0$$

Thus, by the Lax - Milgram Theorem we know there exists a unique weak solution $u_h \in V$ to (3.12). $\square$

If we take $\{v_1, v_2, ..., v_N\}$ to be the piecewise linear functions in $H_0^1(\Omega)$ which are globally continuous, regular, and

$$v_i(p_k) = \begin{cases} 1 & : p_k \in T_j \\ 0 & : p_k \notin T_j \end{cases}$$

where $k = 1, 2, 3$ and $i = 1, ..., N$ then

$$\tilde{u}_j(p_k) = \sum_i^N \tilde{u}_i v_i(p_k) \tag{3.11}$$

At this point we will assume v_i is always a function of p_k and denote it as v_i. Substituting this into the weak form we obtain

$$\int_\Omega (D\nabla_s \sum_i^N \tilde{u}_i v_i + Dq \sum_i^N \tilde{u}_i v_i \nabla_s \phi) \cdot \nabla_s v \, ds = -Dq\bar{u} \int_\Omega \nabla_s \phi \cdot \nabla_s v \, ds$$

Letting Ω be represented as its decomposition of triangular faces T_j gives us

$$\sum_j \int_{T_j} (D \sum_i \tilde{u}_i \nabla_s v_i \cdot \nabla_s v_j + Dq \sum_i \tilde{u}_i v_i \nabla_s \phi \cdot \nabla_s v_j) \, ds = -Dq\bar{u} \sum_j \int_{T_j} \nabla_s \phi \cdot \nabla_s v_j \, ds$$

factoring the u_i out give us

$$\sum_j \int_{T_j} (D \sum_i \nabla_s v_i \cdot \nabla_s v_j + Dq \sum_i v_i \nabla_s \phi \cdot \nabla_s v_j) \, ds \; \tilde{u}_i = -Dq\bar{u} \sum_j \int_{T_j} \nabla_s \phi \cdot \nabla_s v_j \, ds$$

and by rearranging the sums

$$\sum_j \sum_i \int_{T_j} (D\nabla_s v_i \cdot \nabla_s v_j + Dq v_i \nabla_s \phi \cdot \nabla_s v_j) \, ds \; \tilde{u}_i = -Dq\bar{u} \sum_j \int_{T_j} \nabla_s \phi \cdot \nabla_s v_j \, ds \tag{3.12}$$

We now we have an equation in the form $(A + B)\tilde{u} = b$ where

$$A_{j,i} = D \int_{T_j} \nabla_s v_i \cdot \nabla_s v_j \, ds \tag{3.13}$$

$$B_{j,i} = Dq \int_{T_j} v_i \nabla_s \phi \cdot \nabla_s v_j \, ds \tag{3.14}$$

$$b_j = -Dq\bar{u} \int_{T_j} \nabla_s \phi \cdot \nabla_s v_j \, ds \tag{3.15}$$

To preform the integration needed for each entry of A, B and b we use a gaussian quadrature method on the surface. This requires an effective way of evaluating the basis functions v_i. To do this we move to the reference element.

3.3 Reference Element

The reference element refers to the triangle with vertices at

$$p_1 = (0,0,0), \;\; p_2 = (1,0,0), \;\; p_3 = (0,1,0) \tag{3.16}$$

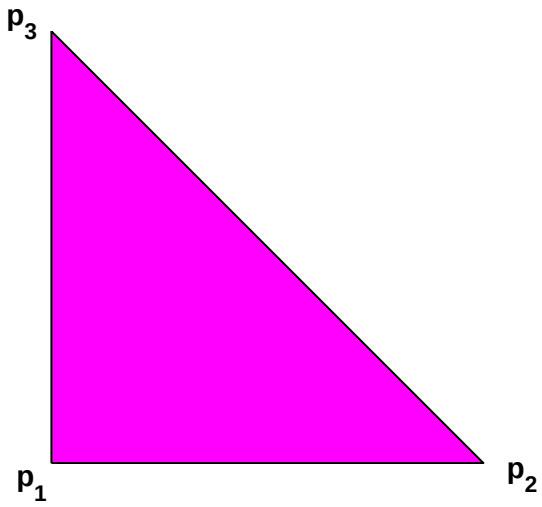

Figure 3.2: Reference Triangle

To distinguish between reference triangle elements and physical triangle elements. We will denote the reference elements with coordinates (ξ, η, ζ) and physical elements with coordinates (x, y, z). Also note the cooresponding node indicies will be labled in a counter-clockwise order. Since our reference triangle lies on the $xy - plane$ we can treat it in two dimensions with the following local basis functions

$$N_1 = 1 - \xi - \eta, \;\; N_2 = \xi, \;\; N_3 = \eta \tag{3.17}$$

with surface gradients

$$\nabla_s N_1 = \begin{bmatrix} -1 \\ -1 \\ 0 \end{bmatrix}, \;\; \nabla_s N_2 = \begin{bmatrix} 1 \\ 0 \\ 0 \end{bmatrix}, \;\; \nabla_s N_3 = \begin{bmatrix} 0 \\ 1 \\ 0 \end{bmatrix}, \tag{3.18}$$

This leads to the following affine transformation, denoted as $F(\xi, \eta, \zeta)$, that will take our reference nodes and transform them to the physical nodes

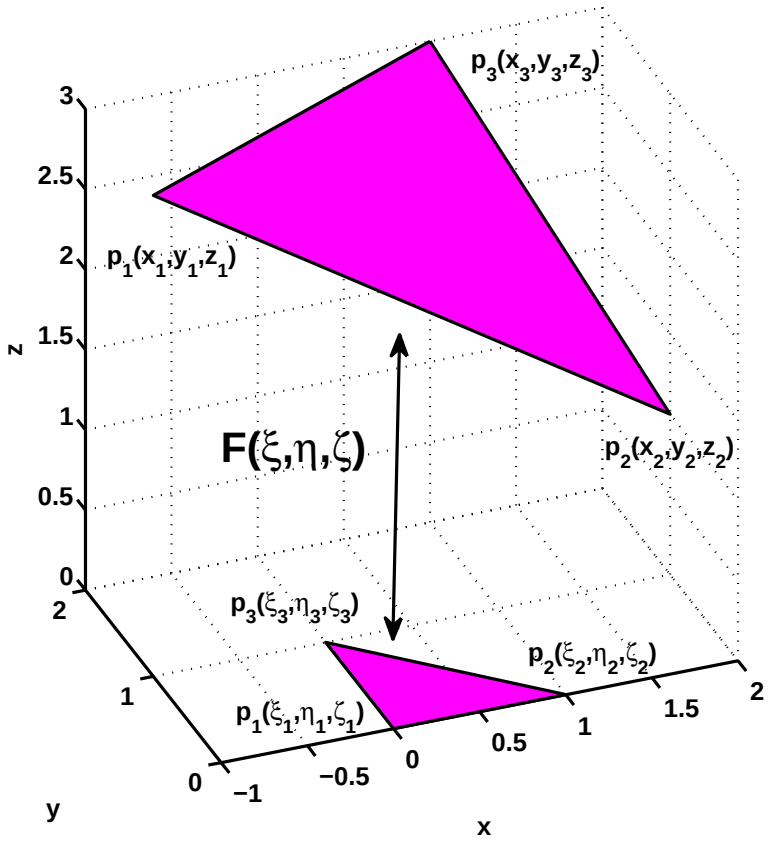

Figure 3.3: Transformation where $\zeta_1 = \zeta_2 = \zeta_3 = 0$

$$\underbrace{\begin{bmatrix} x \\ y \\ z \end{bmatrix} = \underbrace{\begin{bmatrix} x_2 - x_1 & x_3 - x_1 & n_1 \\ y_2 - y_1 & y_3 - y_1 & n_2 \\ z_2 - z_1 & z_3 - z_1 & n_3 \end{bmatrix}}_{\mathrm{M}} \begin{bmatrix} \xi \\ \eta \\ \zeta \end{bmatrix} + \begin{bmatrix} x_1 \\ y_1 \\ z_1 \end{bmatrix}}_{\mathrm{F}(\xi,\eta,\zeta)} \tag{3.19}$$

where n_k are the entries of the normal vector to the triangle T_j and (x_1, y_1, z_1) are the coordinates of the first node on the physical triangle. Now we are able to easliy evaluate the basis functions v_i for each physical triangle.

$$v_i(p_k) = N_i \circ F^{-1}(p_k) \tag{3.20}$$

To find the surface gradients of $\nabla_s v_i$ we use the transformation matrix, M, and applying the chain rule gives us

$$\nabla_s v_i = M^{-T}(\nabla_s N_i \circ F^{-1}(p_k)) \tag{3.21}$$

Note that since $\nabla_s N_i$ is constant we do not need to evaluate $\nabla_s N_i$ at $F^{-1}(p_k)$ leaving us with the simple expression

$$\nabla_s v_i = M^{-T}(\nabla_s N_i) \tag{3.22}$$

3.4 Quadrature

We can now numerically integrate using a 4-point Gauss Quadrature scheme. Which consists in replacing the integrals with a finite sum as follows

$$A_{j,i} = D \int_{T_j} \nabla_s v_i \cdot \nabla_s v_j \, ds \approx \sum_{l=1}^{4} \omega_l \nabla_s v_i(h_l) \cdot \nabla_s v_j(h_l) \tag{3.23}$$

$$B_{j,i} = Dq \int_{T_j} v_i \nabla_s \phi \cdot \nabla_s v_j \, ds \approx \sum_{l=1}^{4} \omega_l v_i \nabla_s \phi(h_l) \cdot \nabla_s v_j(h_l) \tag{3.24}$$

$$b_j = -Dq\bar{u}\int_{T_j} \nabla_s\phi\cdot\nabla_s v_j\, ds \approx -\bar{u}\sum_{l=1}^{4}\omega_l\nabla_s\phi(h_l)\cdot\nabla_s v_j(h_l) \tag{3.25}$$

Where ω_l are the weights and h_l are the nodes of the quadrature formula. Note that since $\nabla_s v_j$ are constant there is no need for evaluation at h_l, and this quadrature scheme becomes very simple. For the 4-point gauss quadrature h_l and ω_l are as follows

h_l	ω_l
(1/3,1/3,0)	-0.28125
(1/5,1/5,0)	.26041667
(3/5,1/5,0)	.26041667
(1/5,3/5,0)	.26041667

We can now calculate each entry in A, B, and b and we can numerically solve the system $(A+B)\tilde{u} = b$ by using a linear solver such at the BiConjugate Gradient Method. This results in a family of solutions all differing by a constant. Thus to arrive at the correct solution we must implement a constraint.

3.5 Integration Constant

By implementing the Slotboom variables [8]

$$\hat{D} = De^{-q\phi}\ , \quad \hat{u} = \tilde{u}e^{q\phi} \tag{3.26}$$

the electrodiffusion equation can be transformed to

$$\nabla_s\cdot(\hat{D}\nabla_s\hat{u}) - \frac{\partial(\hat{u}e^{-q\phi})}{\partial t} = -Dq\bar{u}\nabla_s^2\phi \tag{3.27}$$

Since we are considering the steady state problem $\frac{\partial(\hat{u}e^{-q\phi})}{\partial t} = 0$ and we are left with the equation

$$\nabla_s\cdot(\hat{D}\nabla_s\hat{u}) = -Dq\bar{u}\nabla_s^2\phi \tag{3.28}$$

With the constraint

$$\int_{\Omega} \tilde{u}\, ds = 0 \tag{3.29}$$

We know the analytical solution to this problem is $\tilde{u}e^{q\phi}$. Now by adding any constant C to this solution, we also get a solution. So if we make the substitution $\tilde{u}e^{q\phi} + C = \hat{u}$ and factoring out $e^{q\phi}$ to get the desired solution form

$$(\tilde{u} + Ce^{-q\phi})e^{q\phi}$$

We get the following constraint

$$\int_{\Omega} (\tilde{u} + Ce^{-q\phi})\, ds = 0$$

Solving for C we obtain

$$C = \frac{-\int_{\Omega} \tilde{u}\, ds}{\int_{\Omega} e^{-q\phi}\, ds} \tag{3.30}$$

And we get the following unique solution

$$u = \tilde{u} + Ce^{-q\phi} + \bar{u} \tag{3.31}$$

3.6 Numerical Convergence

Because ϕ can be large the linear solver can diverge. The solution then can not be obtained. To solve this problem we have implemented a matrix hacking technique, this guarantees the convergence of the linear solver. To implement this we set a row in the stiffness matrix, $A + B$, equal to zero except at position, (k, j), which is an arbitrary chosen

position

$$A+B=\begin{bmatrix} \vdots & \vdots & \vdots & \vdots \\ a_{k-1,j-1}+b_{k-1,j-1} & a_{k-1,j}+b_{k-1,j} & a_{k-1,j+1}+b_{k-1,j+1} & a_{k-1,j+2}+b_{k-1,j+2}\ldots \\ 0 & 1 & 0 & 0\ldots \\ a_{k+1,j-1}+b_{k+1,j-1} & a_{k+1,j}+b_{k+1,j} & a_{k+1,j+1}+b_{k+1,j+1} & a_{k+1,j+2}+b_{k+1,j+2}\ldots \\ \vdots & \vdots & \vdots & \vdots \end{bmatrix}$$

and set the k^{th} position in f equal to m, some constant.

$$f=\begin{bmatrix} \vdots \\ f_{k-1} \\ m \\ f_{k+1} \\ \vdots \end{bmatrix}$$

To get accurate results one should pick m close to the anticipated solution.

Chapter 4

NUMERICAL SIMULATIONS

In this section we numerically implement the electrodiffusion equations presented above. To test our code we also use three other examples with simple solutions to test for error convergence. We use the Coulomb potential, $\phi = \frac{q}{|x - x_0|}$, where $x_0 = (0, 0, 1.5)$. After we reach a sufficient error threshhold we run the code on a test mesh, to check our code for robustness. Numerically we are interested in the stability of our model, so we have implemented a stability scheme to provide better stability of our model. The coding of the model was done in C++, using the BiConguate Gradient Method and a 4-point Gaussian Quadrature.

4.1 Numerical Examples with Polynomial Solutions

We have implemented the electrodiffusion equations presented above, denoted as *Example* 1. We also look at three other polynomial examples , $u = xy$, $u = zy$, $u = xyz$, as well to test for error convergence. All tests were ran on the unit sphere centered at the orgin with $q = -0.1$. In all cases we get second order convergence, which is diplayed below in Figure 4.1. and Table 4.1.

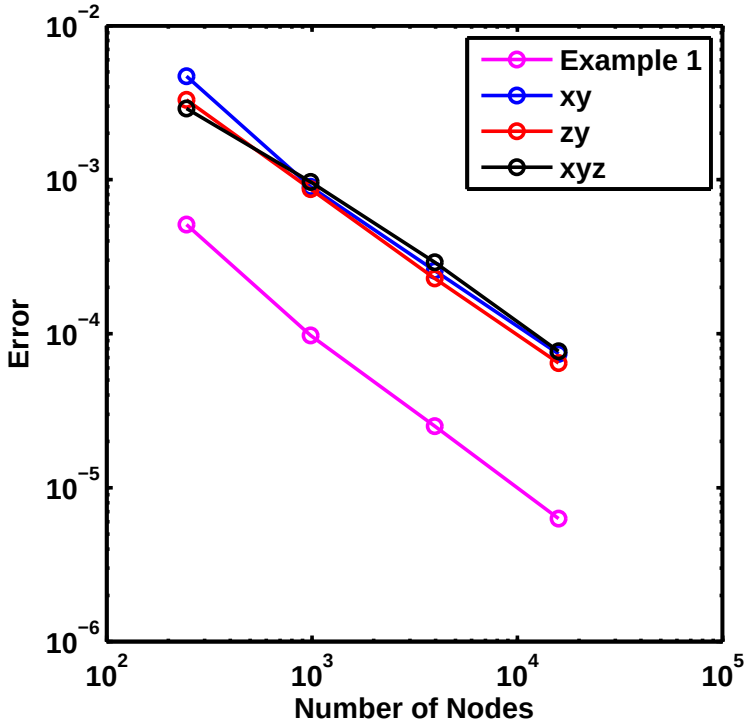

Figure 4.1: Error Convergence for All Examples wtih $q = -0.1$

Table 4.1: Errors for all Test Problems where RC is the Rate of Convergence

$\#of Nodes$	$Example\,1$	RC	$u = xy$	RC	$u = zy$	RC	$u = xyz$	RC
245	5.12E-04		0.0047		0.0033		0.0029	
984	9.73E-05	2.40	9.00E-04	2.38	8.67E-04	1.93	9.65E-04	1.59
3963	2.51E-05	1.95	2.57E-04	1.81	2.29E-04	1.92	2.90E-04	1.73
15910	6.29E-06	2.00	7.40E-05	1.80	6.45E-05	1.83	7.68E-05	1.92

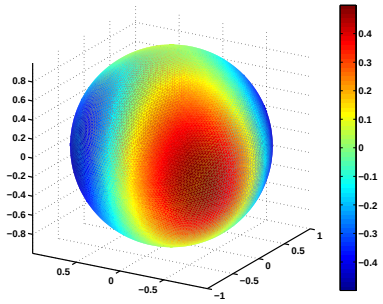

Figure 4.2: Solution for u = xy

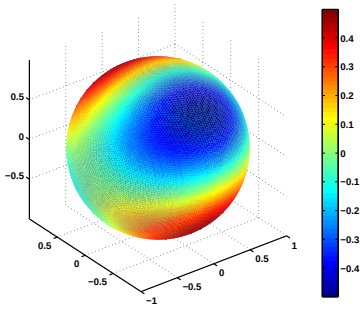

Figure 4.3: Solution for u = zy

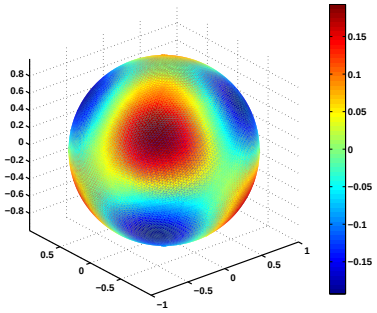

Figure 4.4: Solution for u = xyz

4.2 Numerical Examples with Exponential Solutions

We are interested in what happens as the charge, q, changes in our electrostatic potential. These results can be found in Figure 4.5 and Table 4.2. The errors do go up for larger q which is to be expected, but we still get second order convergence for all q values. The largest error occurs closest to the potential, which is seen in Figure 4.3.

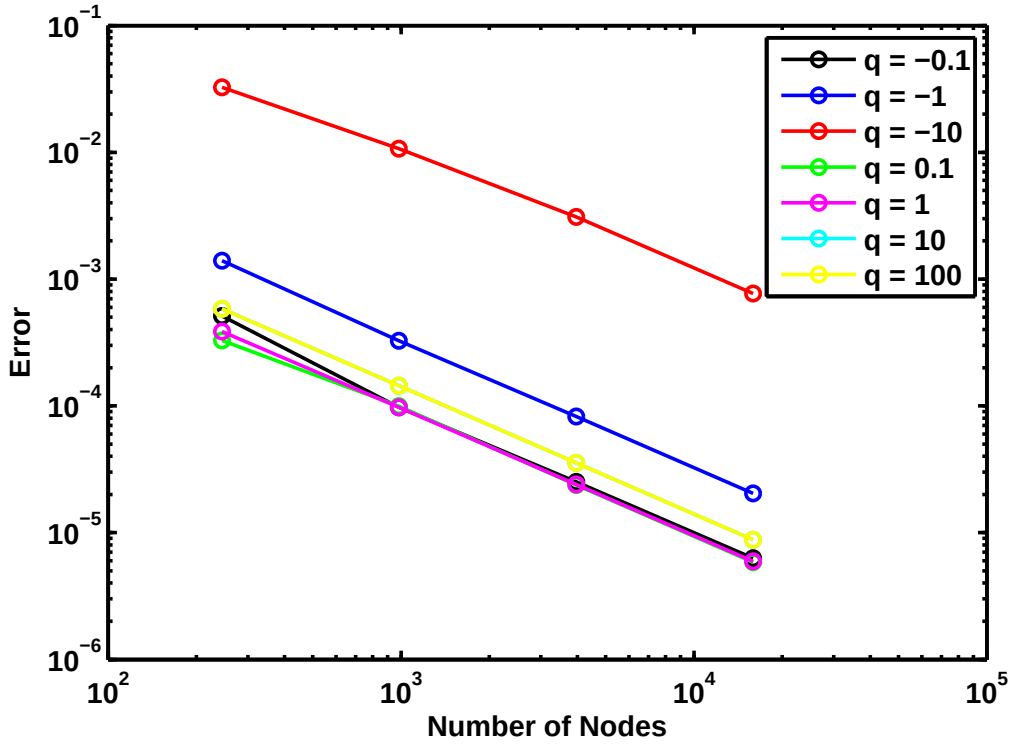

Figure 4.5: Errors for *Example* 1 with different q values

Table 4.2: Errors for *Example* 1 with different q where RC is the Rate of Convergence

$\#of Nodes$	$q=-0.1$	RC	$q=-1$	RC	$q=-10$	RC	$q=0.1$	RC	$q=1$	RC	$q=10$	RC
245	5.12E-04		1.40E-03		0.0325		3.28E-04		3.86E-04		5.83E-04	
984	9.73E-05	2.40	3.27E-04	2.10	1.07E-02	1.60	9.96E-05	1.72	9.74E-05	1.99	1.44E-04	2.02
3963	2.51E-05	1.95	8.23E-05	1.99	3.10E-03	1.79	2.37E-05	2.07	2.39E-05	2.02	3.55E-05	2.02
15910	6.29E-06	2.00	2.04E-05	2.01	7.70E-04	2.01	5.85E-06	2.02	5.94E-06	2.01	8.79E-06	2.01

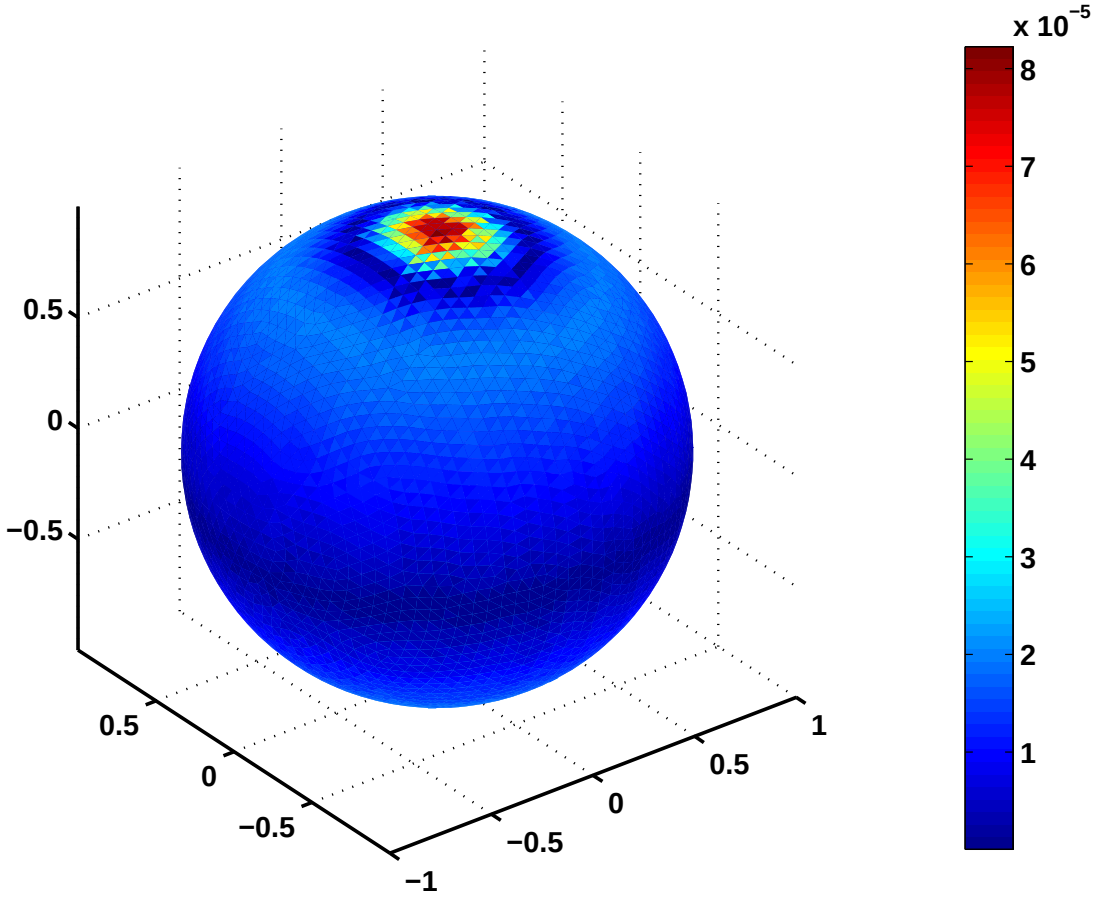

Figure 4.6: Largest error occurs close to ϕ at $z = 1.5$ with 3963 nodes

To check the robustness of the code, we solved the equation on a surface with varying curvature as given in Figure 4.7. The errors of the numerical solutions follow in Figure 4.8 and Table 4.3.

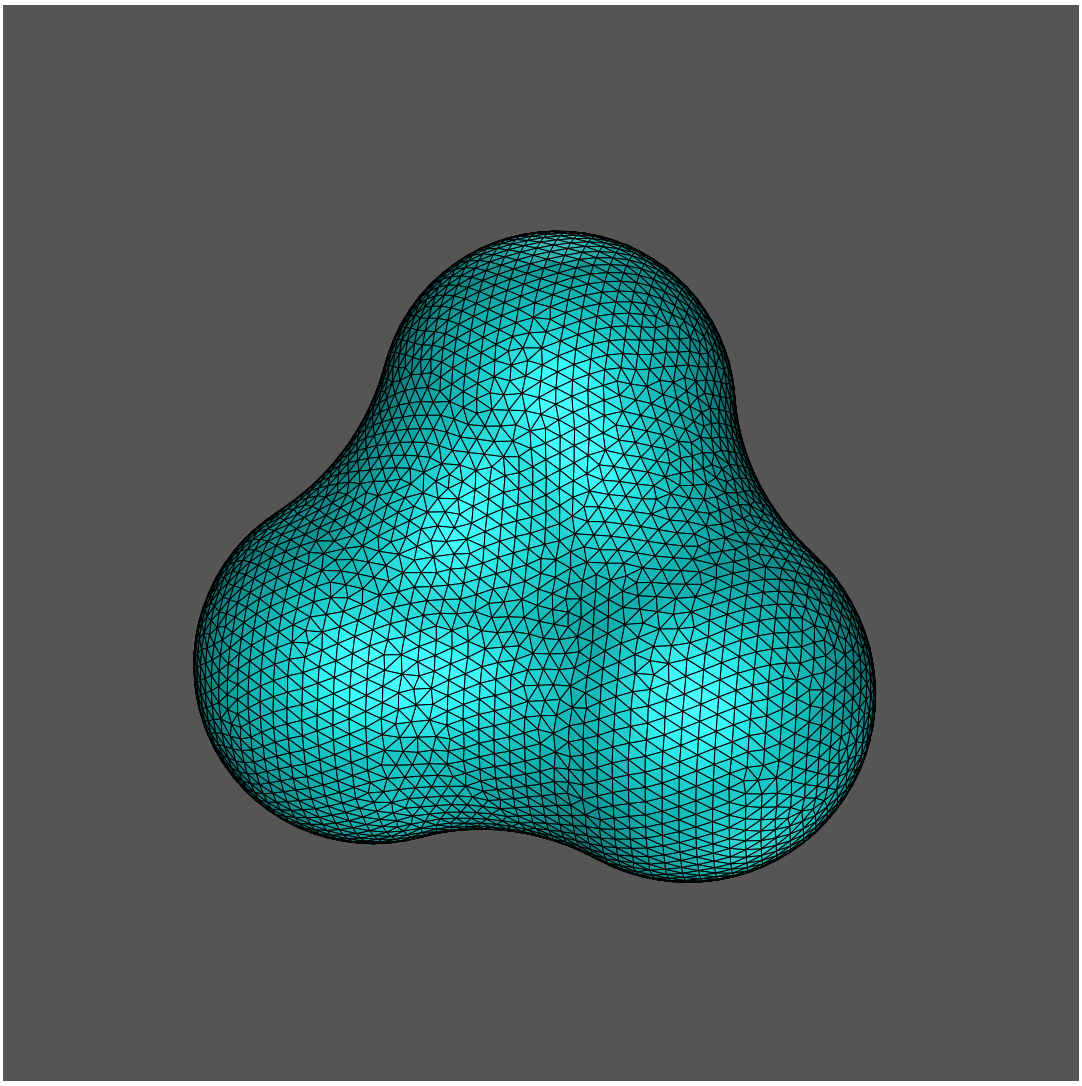

Figure 4.7: Mesh of surface with varying curvature

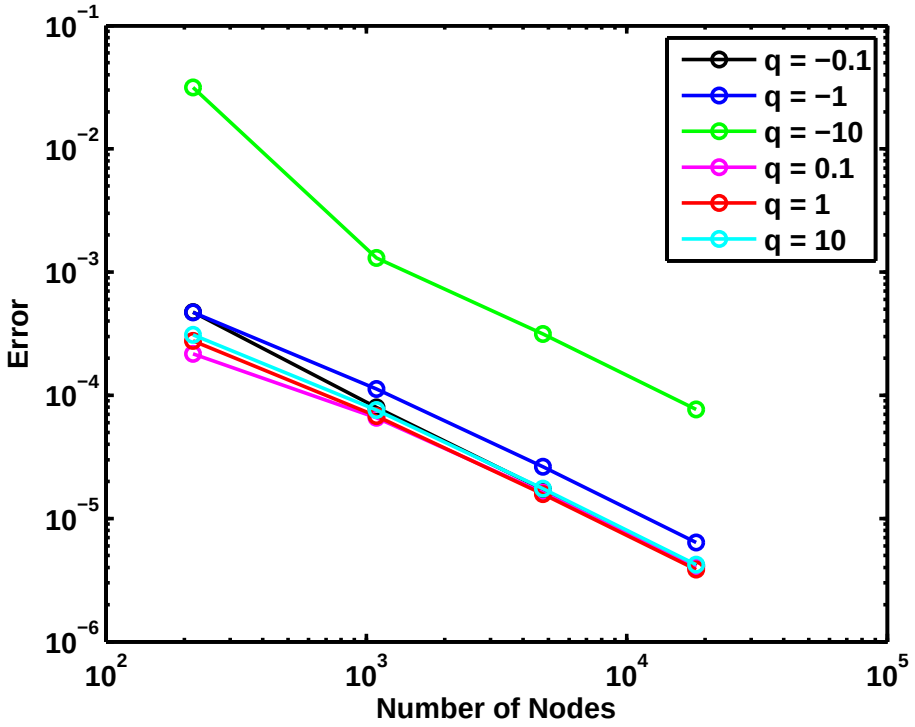

Figure 4.8: Errors for *Example* 1 on surface with varying curvature

Table 4.3: Errors for *Example* 1 with different q on surface with varying curvature where RC is the Rate of Convergence

$\#of Nodes$	$q=-0.1$	RC	$q=-1$	RC	$q=-10$	RC	$q=0.1$	RC	$q=1$	RC	$q=10$	RC
216	4.74E-04		4.71E-04		0.0315		2.17E-04		2.76E-04		3.10E-04	
1094	7.98E-05	2.57	1.12E-04	2.07	1.30E-03	4.60	6.56E-05	1.73	6.77E-05	2.03	7.59E-05	2.03
4761	1.72E-05	2.21	2.63E-05	2.10	3.14E-04	2.05	1.62E-05	2.01	1.58E-05	2.10	1.75E-05	2.12
19473	4.14E-06	2.06	6.38E-05	2.04	7.69E-05	2.03	4.03E-06	2.01	3.86E-06	2.03	4.23E-06	2.04

4.3 Stabilization

For large q values the electrodiffusion equation becomes drift dominated which can result in areas of negative concentration shown in Figure 4.9. This is not physical, so to avoid this

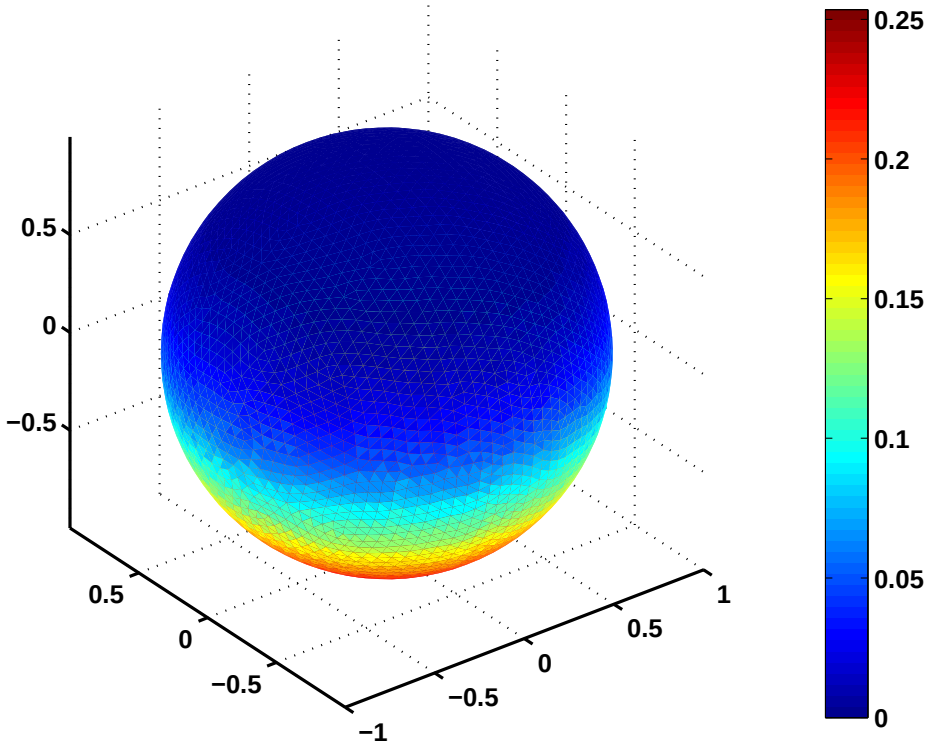

Figure 4.9: $q = -10$ results in negative concentration near ϕ

we add a stabilizing term using Streamline Upwind Petrov-Galerkin (SUPG) equations for stability. These equations are as follows, which are discussed more in [2]

$$v_{supg} = \sigma b \cdot \nabla_s v \tag{4.1}$$

$$\sigma = \frac{e_{max}}{2b}\psi(Pe) \tag{4.2}$$

$$b = -D\nabla_s\phi \tag{4.3}$$

$$\psi(Pe) = \begin{cases} 1 \quad , & \frac{0.33\|b\|_2 e_{max}}{2D} > 1 \\ \frac{0.33\|b\|_2 e_{max}}{2D} \quad , & otherwise \end{cases} \tag{4.4}$$

Where e_{max} is the longest triangle edge. Adding these to the weak form, we have the equation

$$\begin{aligned} &\int_\Omega (D\nabla_s\tilde{u}\cdot\nabla_s v + Dq\tilde{u}\nabla_s\phi\cdot\nabla_s v)\,ds + \int_\Omega (D\nabla_s\tilde{u}\cdot\nabla_s v_{supg} + Dq\tilde{u}\nabla_s\phi\cdot\nabla_s v_{supg})\,ds = \\ &\qquad -Dq\bar{u}\int_\Omega \nabla_s\phi\cdot\nabla_s v\,ds - Dq\bar{u}\int_\Omega \nabla_s\phi\cdot\nabla_s v_{supg}\,ds \\ &\int_\Omega \tilde{u}\,ds = 0 \end{aligned} \tag{4.5}$$

Implementing this, we have the error results found in Figure 4.10 and Table 4.4 which compares the stabilization problem with the original problem.

Table 4.4: Errors for *Example* 1 with and without Stabilization where RC is the Rate of Convergence

$\#ofNodes$	$q=-0.1$	RC	$q=-1$	RC	$q=-10$	RC	$q=0.1$	RC	$q=1$	RC	$q=10$	RC
W/O Stab.												
245	5.12E-04		1.40E-03		0.0325		3.28E-04		3.86E-04		5.83E-04	
984	9.73E-05	2.40	3.27E-04	2.10	1.07E-02	1.60	9.96E-05	1.72	9.74E-05	1.99	1.44E-04	2.02
3963	2.51E-05	1.95	8.23E-05	1.99	3.10E-03	1.79	2.37E-05	2.07	2.39E-05	2.02	3.55E-05	2.02
15910	6.29E-06	2.00	2.04E-05	2.01	7.70E-04	2.01	5.85E-06	2.02	5.94E-06	2.01	8.79E-06	2.01
With Stab.												
245	4.63E-04		0.0122		0.1129		2.55E-04		5.39E-04		0.0292	
984	8.17E-05	2.50	0.002	2.61	0.0786	5.22	7.99E-05	1.67	1.34E-04	2.01	0.0069	2.08
3963	2.17E-05	1.91	5.69E-04	1.81	0.0258	1.61	1.90E-05	2.07	3.50E-05	1.93	0.0019	1.86
15910	5.49E-06	1.99	1.62E-04	1.81	0.0072	1.84	4.71E-06	2.01	9.76E-06	1.84	5.78E-04	1.72

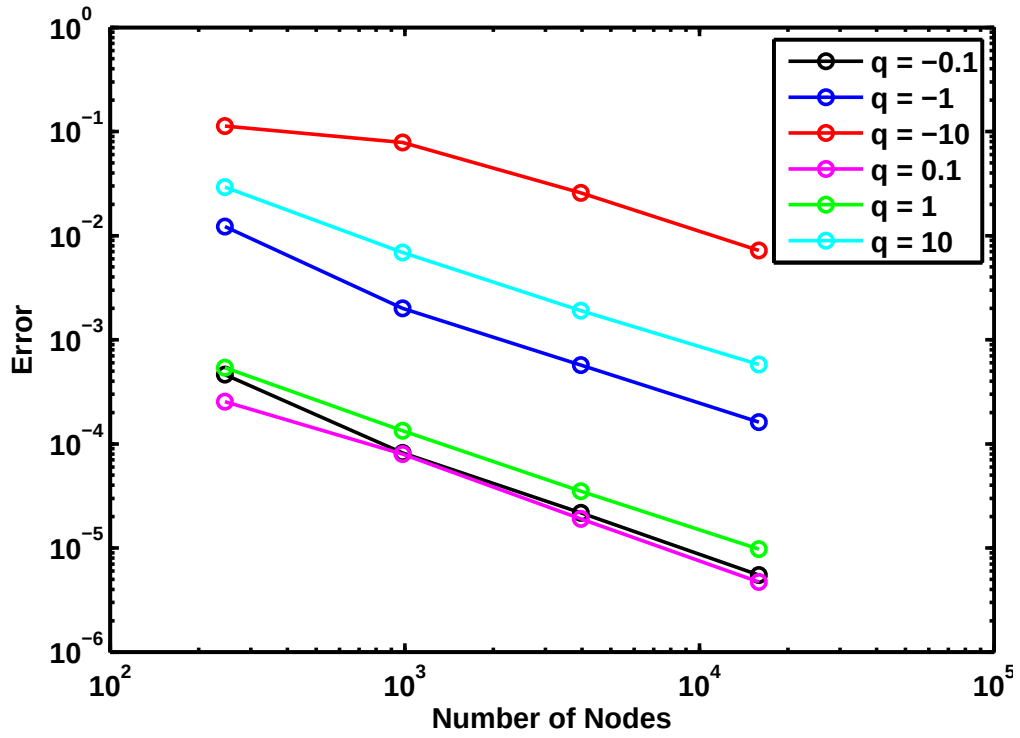

Figure 4.10: Errors for *Example* 1 with Stabilization

The errors increase as q increases, but stay relatively small for smaller q. For larger q such as $q = 100$ the linear solver for the original problem did not converge, but with the added stabilization term the linear solver does converge. We tested the stabilization problem for rubustness as well by running the Test Mesh presented above. The results are found in Figure 4.11 and Table 4.5

Table 4.5: Errors for Example 1 with Stabilization ran on Test Mesh where RC is the Rate of Convergence

$\#of Nodes$	$q = -0.1$	RC	$q = -1$	RC	$q = -10$	RC	$q = 0.1$	RC	$q = 1$	RC	$q = 10$	RC
216	8.16E-04		0.0085		0.0536		2.26E-04		4.09E-04		0.017	
1094	1.11E-04	2.88	0.0012	2.82	0.005	3.42	7.17E-05	1.65	9.23E-05	2.15	0.003	2.50
4761	2.30E-05	2.27	2.29E-04	2.39	0.0015	1.74	1.79E-05	2.01	2.14E-05	2.11	6.90E-04	2.12
19473	5.46E-06	2.07	5.17E-05	2.15	3.42E-04	2.13	4.43E-06	2.01	5.07E-06	2.08	1.52E-04	2.18

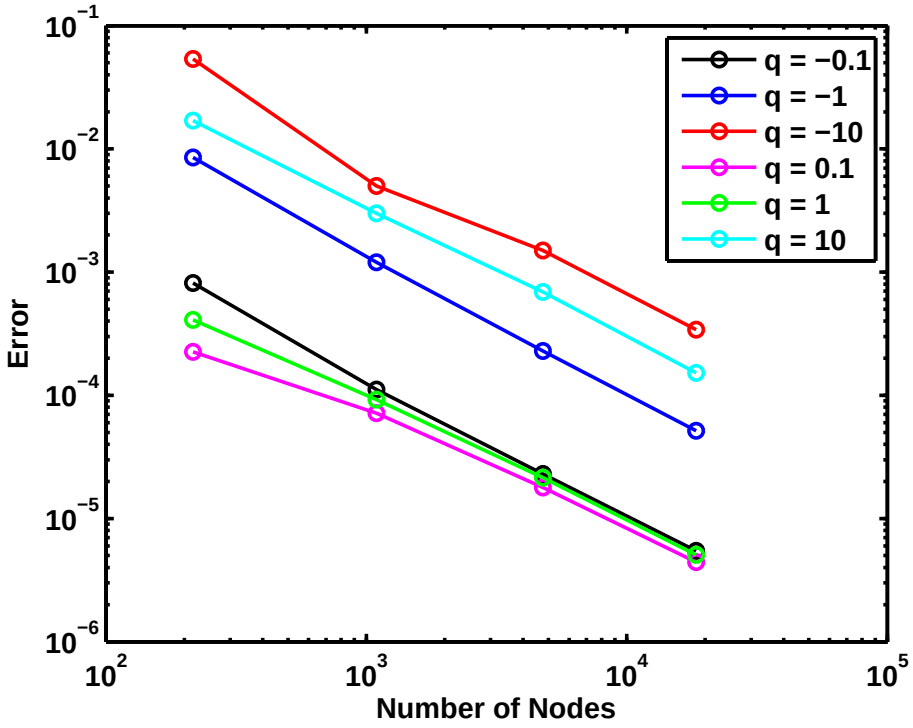

Figure 4.11: *Example* 1 with Stabilization ran on Test Mesh

Chapter 5

CONCLUSIONS

5.1 Future Work

One draw back to the electrodiffusion equation that I have presented is that it allows for infinite concentration of lipids on the memebrane surface. This result is not physical, since lipids have a finite size [15]. The next step in my research will be to implement the addition of a term that will omit this concentration problem. The new equation will be

$$\nabla_s \cdot D\left(\nabla_s u + \frac{ua^2\nabla_s u}{1-a^2u} + qu\nabla_s\phi\right) = 0 \tag{5.1}$$

where a is the effective size of the lipid. In addition to this, the equation I have presented assumes that ϕ is given. We can in fact calculate ϕ by using the Poisson equation

$$-\nabla\cdot(\epsilon\nabla\phi) = \sum_i q_i\delta(x_i) + \sum_j q_j\rho_j \tag{5.2}$$

where q_i is the charge at x_i, and ρ_j is the concentration of distributed charges with valence q_j [15]. This charge distribution can be described as an interface condition on $\Omega = \Omega_s \cup \Omega_m$ as seen in Figure 5.1. By coupling this with equation 5.1 we obtain

$$\begin{aligned} &\nabla_s \cdot D\left(\nabla_s u + \frac{ua^3\nabla_s u}{1-a^3u} + qu\nabla_s\phi\right) = 0 \\ &\phi_m = \phi_s\ ,\ \epsilon_m\frac{\partial\phi_m}{\partial n} = \epsilon_s\frac{\partial\phi_s}{\partial n} + uq \end{aligned} \tag{5.3}$$

where ϵ_s and ϵ_m are dielectric permittivity constants. This can be obtained by using variations of the free energy functional, F, as in equation 2.2, with respect to ϕ. This is further discussed in [8]. This model can be even better if we allow for multiple types of lipids on the

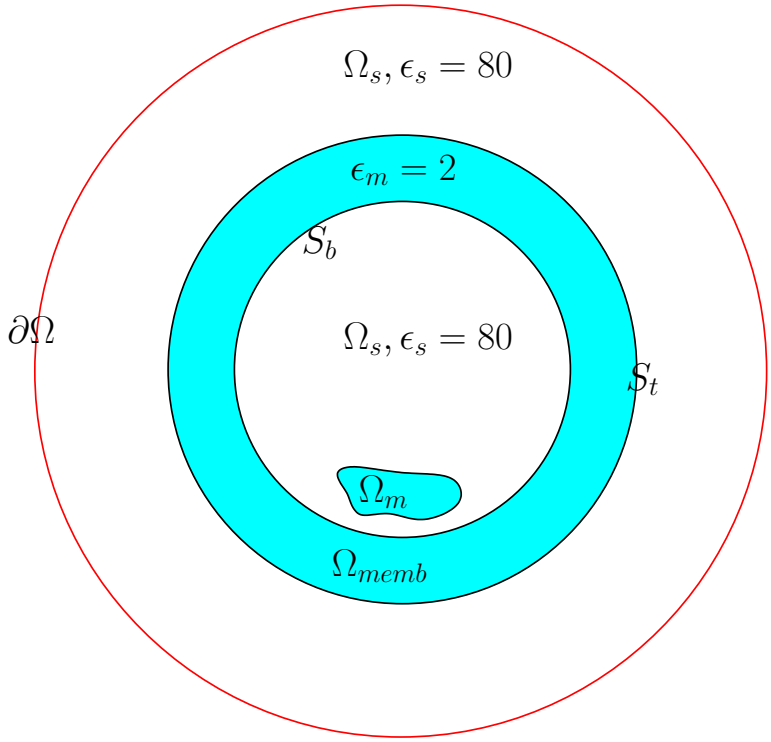

Figure 5.1: 2D cross section of the computational model. The domain Ω_{memb} is the bilayer membrane modeled as a dielectric continuum without atomistic details. Distribution of lipids on membrane surfaces S_t and S_b follows the surface electrodiffusion equation. Mobile ions are distributed in the aqueous solution exterior and interior to the vesicle. Atomistic structure of the MARCKS peptide is retained and singular charges are distributed in Ω_m . $\partial\Omega$ is the boundary of the computational domain.

surface of the membrane. This is accomplished through a system of equations where each component consists of solving the electrodiffusion equation for each type of lipid. We will then investigate the stability of the model by implementing an exponential fitting scheme like that discussed in [4]. Although this equation has a lower bound on the solution for the continuous problem there lacks a proof for a lower bound on the discrete solution to equation 5.3. This will also be a necessary task in the implementation of this model.

The equation I have given in this paper is posed on a nice smooth static surface, however cell membranes are very pliable and are constantly changing shape. It is very necessary then to consider a deforming surface with a membrane velocity. This will require an additional term to account for the surface deformation. One way to do this is presented by Holmes in [6] and discussed briefly in section 2.1.3.

One of the greatest biological phenomena is the flip-flop movement of lipids on a bilayer membrane. It is difficult to understand how and why a hydrophilic lipid head flips over a hydrophobic bilayer. Not only is it difficult to understand, but even more difficult to model. This effect has many degrees of freedom which make it hard, maybe even impossible, to model. Although this task is a difficult one, over time we hope to implement a model that will effectively describe this physical phenomenon.

5.2 Summary

The modeling of the cell membrane is an essential task that will not only improve our knowledge of the cell itself but allow us to apply the knowledge to enhance the delivery of nutrients needed to the cell. The electrodiffusion equations presented are a strong theoretically proven model for the movement of lipids on bilayer membrane surfaces. With the existence and uniqueness of solutions this model is well defined as well as usable. The surface linear finite element method offers a strong numerical solution to the electrodiffusion equations with the use of the decomposition, and the matrix hacking technique. We have developed a working C++ code that numerically solves electrodiffusion on surfaces, and produces excellent results. This model produces a physical solution, even in the presence of a large electropotential, where other models and numerical techniques fail. This model is a good base that allows for many other advanced models to be built from it and opens up the possibiliy for further research in this area.

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